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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/824,597	04/15/2004	Stephen J. Pandol	034047.021.1	7147

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EXAMINER	
PAGONAKIS, ANNA	
ART UNIT	PAPER NUMBER
4173	
MAIL DATE	DELIVERY MODE
11/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/824,597	PANDOL ET AL.	
	Examiner	Art Unit	
	Anna Pagonakis	4173	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *05 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5; 11-17; 20-24 and 36* is/are pending in the application.

4a) Of the above claim(s) *6-10; 18-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5; 11-17; 20-24 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group I, claims 1-24, in the reply field on 9/5/2007 is acknowledged. The addition of claim 25 is acknowledged

Claims 1-5; 11-17; 20-24 and 36 are currently pending and are the subject of this Office Action.

Claims 6-10; 18-19 are withdrawn from consideration as being drawn to non-elected subject matter.

This is the first Office Action on the merits of the application.

Change of Examiner

The examiner assigned to the instant application has changed. The new examiner is Anna Pagonakis. Contact information is provided at the end of the office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The term "modulating" in claims 1-5; 11-17; 20-24 and 36 is a relative term, which renders the claim indefinite. The term "modulating" is not defined by the claim and the specification fails to specify the effect that is intended from the administration of these claimed compounds. The word "modulating" embraces a variety of effects, which applicants have failed to concisely define in the instant claims to the skilled artisan. In particular, "modulating" can be decreasing, increasing 100% inhibition, or even potentiation of the neoplastic growth, does not

provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 1-5; 2, 21, 24 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The use of the designation "PKC" renders the claims indefinite as the recitation is too vague. "PKC" is a simple acronym/abbreviation that has many different meanings in the art and thus the inclusion thereof is confusing and the claims indefinite. Applicant should simply spell out the full name of the receptor in at least the first occurrence to obviate this rejection.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. The term "derivative" in claim 12 is a relative term that renders the claim indefinite. In particular, the term "derivative" does not particularly point out the degree or type of derivation that a given compound may have in relation to the parent compound and still be considered a "derivative" as intended by Applicant. Applicant has failed to provide any specific definition for these terms in the present specification. Lacking a clear meaning of the term "derivative," the skilled artisan would not be reasonably apprised of the metes and bounds of the subject matter for which Applicant seeks patent protection. Words and phrases in the claims must be given their "plain meaning" as understood by one having ordinary skill in the art unless defined by

Applicant in the specification with "reasonably clarity, deliberateness and precision" (MPEP 2111.01). Here, Applicants' definition of "derivative" is not reasonably clear, deliberate or precise because the mere statement of the use of an analog or a derivative does not specify what other compounds may be considered rottlerin derivatives. That is, the definition is presented in a non-limiting manner. Thus, the identity of those compounds that are included or excluded by the term "derivative" is open to subjective interpretation and such is inconsistent with the tenor and express requirements of 35 U.S.C. 112, second paragraph.

Claim 20 recites the limitation "the polyphenolic compound" in line 1. There is insufficient antecedent basis for this limitation in claim on which claim is dependent.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Considering that claims 1-5; 11-17; 20-24 and 36 are drawn to a method of treating, preventing, inhibiting or modulating NF-kappaB activation by administering at least one polyphenolic compound, an inhibitor of PKC delta translocation, an inhibitor of PKC epsilon translocation or a combination thereof the said claims are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed method of treating pancreatic cancer and pancreatitis does not reasonably provide enablement for a method to prevent pancreatic cancer or pancreatitis.

The specification does not enable any skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. In Re Wands, 8 USPQ2nd 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph have been described. They are herein discussed in view of the instant invention.

The nature of the invention

Applicant claims a method of treating, preventing, inhibiting or modulating NF-kappaB activation by administering at least one polyphenolic compound, an inhibitor of PKC delta translocation, an inhibitor of PKC epsilon translocation or a combination thereof by administering rottlerin and genistein.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e., what compounds can treat or prevent which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge would prevent one of ordinary skill in the art from accepting any therapeutic or preventative regimen its face. Moreover, there is no prior art disclosing the prevention of said disease.

The instant claimed inventions are highly unpredictable as discussed below: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually

assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the prevention of said disease is highly unpredictable since one skilled in the art would need to carry out experimentation to determine if any of the claimed multiple claimed compositions, are indeed active, Parkinson's disease and if as a consequence, the said treatments can be achieved. Moreover, the specification lacks to show a method of treating said subjects need to undergo in order to prevent said disease.

The level of skill in the art

The level of skill in the art is high. However, due to the unpredictability of the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine a method of determining the subjects that would certainly suffer from the said conditions or diseases as a method for showing that method wherein the said subjects are subjected to the claimed compounds in order to achieve the claimed prevention.

Thus the specification fails to provide sufficient support for said prevention methods. Thus, one of skill in the art would have to perform an exhaustive experimentation in order to practice the claimed compounds.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2nd 1001, states "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion," and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test whether the said disease can be prevented in instant claims, with no assurances of success.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5; 11-17; 20-24 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Agus et al.

Agus et al. teach that administration of both rottlerin and genistein "significantly inhibited both DNA binding and metabolite formation with ATP" of the known carcinogen 2-amino-3-methylimidazo[4,5-f]quinoline" (abstract). This carcinogen is capable of "inducing tumors in tissues such as liver, small and large intestine, lunge, pancreas and mammary gland" (introduction, lines 4-7).

Though induction of apoptosis or inhibition of nucleic acid synthesis by rottlerin and caspase activation by genistein are not explicitly taught by the references, they are both inherent given that apoptosis and caspase activation are commonly known to occur during administration of an agent aiding in the treatment of cancer or inflammation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5; 11-17; 20-24 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al. (USPGPub 2004/0023925 A1) in view of Glimcher et al (USPGPub2005/0026285).

Chang et al. teaches the administration of genistein (claim 30) to inhibit the growth of a tumor cell including a pancreatic tumor cell (claim 31) which in turn induces mithochondrial dysfunction and/or caspase activation (claim 6).

Glimcher et al. teaches the administration of rottlerin (paragraph [0455]) to cancer including pancreatic cancer (paragraph [0103]).

One of ordinary skill in the art would have been motivated to combine the above references and as combined would teach the invention as claimed. One of ordinary skill in the

art would have been motivated by Chang et al. and Shachar et al. because both are directed to the treatment of cancer. Moreover, administrating agents together which are known to be useful for the treatment of cancer is prima facie obvious. See In re Kerkhoven 205 USPQ 1069. Since it is prima facie obvious to administer these two compounds which are taught by the prior art to be useful for the same purpose, the idea of administering both flows logically from having been individually taught in the prior art.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anna Pagonakis whose telephone number is 571-270-3505. The examiner can normally be reached on Monday thru Thursday, 9am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AP

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614